

<110> Corrado FOGHER

<120> SYNTHETIC POLYNUCLEOTIDE CODING FOR HUMAN LACTOFERRIN, VECTORS, CELLS AND TRANSGENIC PLANTS CONTAINING IT

<130> 4161-14 / X89727RVP

<140> 09/743,823

<141> 2001-08-22

<150> PCT/IT99/00226

<151> 1999-07-19

<150> IT RM98A000478

<151> 1998-07-17

<160> 26

<170> MS Word

<210> 1

<211> 2079

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic human lactoferrin

<220>

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<222> (1)..(2076)

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gcc aca aaa tgc ttc caa tgg caa agg aat atg aga aaa gtt cgt gga 96
Ala Thr Lys Cys Phe Gln Trp Gln Arg Asn Met Arg Lys Val Arg Gly
20 25 30

cct cct gta tct tgc ata aag aga gat tca ccc atc cag tgt atc cag
Pro Pro Val Ser Cys Ile Lys Arg Asp Ser Pro Ile Gln Cys Ile Gln $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$

gca att gcg gaa aac aga gct gat gct gtg act ctt gat ggt ggt ttc 192
Ala Ile Ala Glu Asn Arg Ala Asp Ala Val Thr Leu Asp Gly Gly Phe
50 55 60

ata tac gag gca gga ctt gcc cca tac aaa ctg cga cct gta gcg gcg 240

Ile Tyr Glu Ala Gly Leu Ala Pro Tyr Lys Leu Arg Pro Val Ala Ala
65 70 75 80

gaa gtc tac ggg acc gaa aga caa cca cga act cac tat tat gct gtg 288 Glu Val Tyr Gly Thr Glu Arg Gln Pro Arg Thr His Tyr Tyr Ala Val

•																
				85					90					95		
														caa Gln		336
														aat Asn		384
					_			-			-			cct Pro		432
														gtt Val		480
														gcg Ala 175		528
														ttc Phe		576
			-		_	_		_	_		-			gtt Val		624
ttt	att	aga	gag	agc	aca	gtg	ttt	gag	gat	ctt	tca	gac	gag	gct	gaa	672

Phe Ile Arg Glu Ser Thr Val Phe Glu Asp Leu Ser Asp Glu Ala Glu agg gac gag tat gag tta ctc tgc cca gac aac act cgt aag cca gtt Arg Asp Glu Tyr Glu Leu Leu Cys Pro Asp Asn Thr Arg Lys Pro Val 7.68 gac aag ttc aaa gat tgc cat ctt gca cgg gtc cct tct cat gcc gtt Asp Lys Phe Lys Asp Cys His Leu Ala Arg Val Pro Ser His Ala Val gtg gca cga agt gtt aat gga aag gat gcc atc tgg aat ctt ctc Val Ala Arg Ser Val Asn Gly Lys Glu Asp Ala Ile Trp Asn Leu Leu cgc caa gca cag gaa aag ttt gga aag gac aag tca ccg aaa ttc cag Arg Gln Ala Gln Glu Lys Phe Gly Lys Asp Lys Ser Pro Lys Phe Gln ctc ttt ggt tcc cct agt ggg cag aaa gat ctt ctg ttc aag gac tct Leu Phe Gly Ser Pro Ser Gly Gln Lys Asp Leu Leu Phe Lys Asp Ser gcc att ggg ttt tcg aga gtg cca cct agg ata gat tct ggg ttg tac Ala Ile Gly Phe Ser Arg Val Pro Pro Arg Ile Asp Ser Gly Leu Tyr

				act Thr						1008
				cgt Arg						1056
				tgt Cys						1104
				gcc Ala 375						1152
				gat Asp						1200
				ggt Gly						1248
				gac Asp						1296
				gtg Val						1344
				aaa Lys 455						1392
				aat Asn						1440
_		_		gat Asp	-		_	-	 _	1488
				aat Asn						1536
				gtt Val						1584
				tgc Cys 535						1632

ttt gtg aaa ga Phe Val Lys Aa 545	_										
gag gca tgg go Glu Ala Trp A											
ctc gat ggc as Leu Asp Gly Ly 58			Glu Ala Arg								
gcc atg gcc co Ala Met Ala P: 595											
cgc ttg aaa ca Arg Leu Lys G 610											
gga tot gao to Gly Ser Asp Cy 625											
aac ctt ttg t Asn Leu Leu Pl	_										
aaa aca aca ta Lys Thr Thr Ty			Pro Gln Tyr								
act aat ctg aa Thr Asn Leu Ly 675											
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gattcaccca tccagtgtat ccaggcaatt gcggaaaaca gagctgatgc tgtgactctt 180
gatggtggtt tcatatacga ggcaggactt gccccataca aactgcgacc tgtagcggcg 240
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ctgcgaagtc ctgtgtggca tgacttcaga ccttgaagtt cgttcagctg aaaagatccg 180
cccttcttca caacagccac agcataatag tgagttcgtg gttgtctttc ggtcccgtag 240
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aagacactta aaggcaccag agtagctgaa gtacggttcc tgggatgaga atgcacattt 180
gttttcccct gtccccgcac acaggcgaca aaggttgggg aattgtcctt tatctgcacc 240
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tggaacacaa
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<212> DNA
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tccaaacttt tcctgtgctt ggcggagaag attccagatg gcatcctcct ttccattaac 180
acttcgtgcc acaacggcat gagaagggac ccgtgcaaga tggcaatctt tgaacttgtc 240
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aactggctta cgagt
<210> 12
<211> 251
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<213> Artificial Sequence
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<223> Description of Artificial Sequence: Synthetic DNA
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caettgegea aetettgete teccaeegea caecaaaega eeegegeaeg eegggeagea 180
acttcctcct cacttttcct caagttctga attgcagtaa agtatccgga gccaaggtac 240
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agttgcaata gcgagaaaga ctcctacagg aaccaagcat gccacgctcg ttgcaacctc 180
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aagatateet teeacaggte tateeacaca gttaggatea gggteactge tttgttgtga 180
tttgtagttc tctgcaagac aggcaccaaa ccacatttac ctgcagtgta aacatatcct 240
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ccatccaaac
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gccaagcaac ggaaagcccc agtgtaaccg tagtatctct cgttgctgtt gggaacgcac 120
ttattctcac cttqctcatc tccaatacac aaagcacaga gattagatct tgggtcagaa 180
ccaggggcac agetttgact gaaatattca tcaaatttgc aggagcccgt ctggttgaag 240
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agcaagccca tggg
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<211> 229
<212> DNA
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tctagcttca gtcacaggct tacgtttgcc atcgaggcac agcaacgcaa agtctgcaag 180
cttcaaatcc ttagcccatg cctcattgtt atttccatca gtgttctgc
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<210> 18
<211> 210
<212> DNA
<213> Artificial Sequence
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tctggcaaga cactcagtgt tgtcattgaa caaaaggttt ttggtttcag actggaataa 180
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<211> 30

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<211> 28
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gagetettae tteettagga atteacag
<210> 21
<211> 1367
<212> DNA
<213> Artificial Sequence
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ttttaaggca attaagcatg tttgataaaa tatatatatt gttataaata cttttcaaaa 180
gtataaagtt gatgatggcg tggtggtaga ttattttagt tctaggttcg aatgcaagtt 240
ggtttagaca tttagcctta ttctttttc taaccaaaat aaatgtaaat ggaaaacctt 300
taggaaaaaa aagaaatcaa aattgaaaac atcatccggt ggagtcgaga agcccacacc 360
cacqtqaccc aacaatatta aaataagagt ttgctctaca gtaaatgcga tactttttta 420
ttcaatactt tttccacttc taaaatcttg gagatttgca ccgttaacta attaagtgtt 480
atatccaacg gtcctaaaaa aacttgtgta ccgtgcctca catttcaact ttgcgcaccc 540
tqaaaqccqt tatqtttaqq ttaqtqtttq caacagttga agcgcatcac tcaggaggct 600
acttggtctt gcttttgcgt cttttgttca atttttcacg tgattttgtt ggtgaacacg 660
cgtacttgaa acttattata aattacataa ttttataagt ttcacttctt atataatact 720
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acagagtttc aaacggatga aatctgcatg gcatgcaact aaagcattgt tctcagctgc 1080
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tagccaaacg gtgatctttc tctatatatt gtagctctct aacacaacca acactaccat 1320
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<223> Description of Artificial Sequence: Synthetic DNA
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ataatatat tatattttaa tatctattct tatgtatttt ttaaaaaatct attatatatt 180
gatcaactaa aatatttta tatctacact tattttgcat ttttatcaat tttcttgcgt 240
tttttggcat atttaataat gactattctt taataatcaa tcattattct tacatggtac 300
atattgttgg aaccatatga agtgttcatt gcatttgact atgtggatag tgttttgatc 360
catgcccttc atttgccgct attaattaat ttggtaacag attcgttcta atcagttact 420
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catagcaatg tctaagttca taaaattcaa acaaaaacgc aatcacacac agtggacatc 600
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tcaacccatc atgagcccac acatttgttg tttctaaccc aacctcaaac tcgtattctc 780
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Pro Pro Val Ser Cys Ile Lys Arg Asp Ser Pro Ile Gln Cys Ile Gln
Ala Ile Ala Glu Asn Arg Ala Asp Ala Val Thr Leu Asp Gly Gly Phe
                         55
Ile Tyr Glu Ala Gly Leu Ala Pro Tyr Lys Leu Arg Pro Val Ala Ala
 65
                     70
Glu Val Tyr Gly Thr Glu Arg Gln Pro Arg Thr His Tyr Tyr Ala Val
Ala Val Val Lys Lys Gly Gly Ser Phe Gln Leu Asn Glu Leu Gln Gly
            100
                                105
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Leu Lys Ser Cys His Thr Gly Leu Arg Arg Thr Ala Gly Trp Asn Val Pro Ile Gly Thr Leu Arg Pro Phe Leu Asn Trp Thr Gly Pro Pro Glu Pro Ile Glu Ala Ala Val Ala Arg Phe Phe Ser Ala Ser Cys Val Pro Gly Ala Asp Lys Gly Gln Phe Pro Asn Leu Cys Arg Leu Cys Ala Gly Thr Gly Glu Asn Lys Cys Ala Phe Ser Ser Gln Glu Pro Tyr Phe Ser Tyr Ser Gly Ala Phe Lys Cys Leu Arg Asp Gly Ala Gly Asp Val Ala Phe Ile Arg Glu Ser Thr Val Phe Glu Asp Leu Ser Asp Glu Ala Glu Arg Asp Glu Tyr Glu Leu Leu Cys Pro Asp Asn Thr Arg Lys Pro Val Asp Lys Phe Lys Asp Cys His Leu Ala Arg Val Pro Ser His Ala Val Val Ala Arg Ser Val Asn Gly Lys Glu Asp Ala Ile Trp Asn Leu Leu Arg Gln Ala Gln Glu Lys Phe Gly Lys Asp Lys Ser Pro Lys Phe Gln Leu Phe Gly Ser Pro Ser Gly Gln Lys Asp Leu Leu Phe Lys Asp Ser Ala Ile Gly Phe Ser Arg Val Pro Pro Arg Ile Asp Ser Gly Leu Tyr Leu Gly Ser Gly Tyr Phe Thr Ala Ile Gln Asn Leu Arg Lys Ser Glu Glu Glu Val Ala Ala Arg Arg Ala Arg Val Val Trp Cys Ala Val Gly Glu Gln Glu Leu Arg Lys Cys Asn Gln Trp Ser Gly Leu Ser Glu Gly Ser Val Thr Cys Ser Ser Ala Ser Thr Thr Glu Asp Cys Ile Ala Leu Val Leu Lys Gly Glu Ala Asp Ala Met Ser Leu Asp Gly Gly Tyr Val Tyr Thr Ala Gly Lys Cys Gly Leu Val Pro Val Leu Ala Glu Asn Tyr

Lys Ser Gln Gln Ser Ser Asp Pro Asp Pro Asp Cys Val Asp Arg Pro Val Glu Gly Tyr Leu Ala Val Ala Val Val Val Arg Arg Ser Asp Thr Ser

Leu Thr Trp Asn Ser Val Lys Gly Lys Lys Ser Cys His Thr Ala Val 450 455 460

Asp Arg Thr Ala Gly Trp Asn Ile Pro Met Gly Leu Leu Phe Asn Gln 465 470 475 480

Thr Gly Ser Cys Lys Phe Asp Glu Tyr Phe Ser Gln Ser Cys Ala Pro 485 490 495

Gly Ser Asp Pro Arg Ser Asn Leu Cys Ala Leu Cys Ile Gly Asp Glu 500 505 510

Gln Gly Glu Asn Lys Cys Val Pro Asn Ser Asn Glu Arg Tyr Tyr Gly
515 520 525

Tyr Thr Gly Ala Phe Arg Cys Leu Ala Glu Asn Ala Gly Asp Val Ala 530 540

Phe Val Lys Asp Val Thr Val Leu Gln Asn Thr Asp Gly Asn Asn Asn 545 550 555 560

Glu Ala Trp Ala Lys Asp Leu Lys Leu Ala Asp Phe Ala Leu Leu Cys 565 570 575

Leu Asp Gly Lys Arg Lys Pro Val Thr Glu Ala Arg Ser Cys His Leu 580 585 590

Ala Met Ala Pro Asn His Ala Val Val Ser Arg Met Asp Lys Val Glu 595 600 605

Arg Leu Lys Gln Val Leu Leu His Gln Gln Ala Lys Phe Gly Arg Asn 610 620

Gly Ser Asp Cys Pro Asp Lys Phe Cys Leu Phe Gln Ser Glu Thr Lys 625 630 635 640

Asn Leu Leu Phe Asn Asp Asn Thr Glu Cys Leu Ala Arg Leu His Gly 645 650 655

Lys Thr Thr Tyr Glu Lys Tyr Leu Gly Pro Gln Tyr Val Ala Gly Ile 660 665 670

Thr Asn Leu Lys Lys Cys Ser Thr Ser Pro Leu Leu Glu Ala Cys Glu 675 680 685

Phe Leu Arg Lys 690

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tttttggacc ataagaaaaa gccaaggaac aaaagaagac aaaacacatg agagtatcct 540
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caaatgttca tgcatgttaa caagacctat gactataaat atctgcaatc tcggcccaag 900
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tatattgatc aactaaaata tttttatatc tacacttatt ttgcattttt atcaattttc 240
ttgcgttttt tggcatattt aataatgact attctttaat aattaatcat tattcttaca 300
tegtacatat tgttggaace atatgaagtg tecattgcat tegactatgt ggatagtgtt 360
ttgatccagg cctccatttg ccgcttatta attaatttgg taacagtccg tactaatcag 420
ttacttatcc ttcctccatc ataattaatc ttggtagtct cgaatgccac aacactgact 480
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tcctttgcat agcaatgtct aagttcataa aattcaaaca aaaacgcaat cacacacagt 600
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cccaaaagcc atgcacaaca acacgtactc acaaaggtgt caatcgagca gcccaaaaca 720
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cgtattntnt tccgccacct catttttgtt tattccaaca cccgtcaaac tgcatgccac 840
cccgtggcca aatgtccatg catgttaaca agacctanga ctataaatat ctgcaatctc 900
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taagatatac tatgatgaga gcgcggttcc cattactgtt gctggagttg ttttcctggc 1020
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<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Synthetic signal peptide
Met Ala Ser Ile Leu His Tyr Phe Leu Ala Leu Ser Leu Ser Cys Ser
                                                         15
                                     10
  1
                  5
Phe Leu Phe Phe Leu Ser Asp Ser Val
```

20